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VERSATILE, STEREOCONTROLLED, ASYMMETRIC SYNTHESIS OF E-VINYL GLYCINE DERIVATIVES

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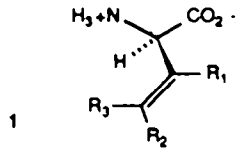
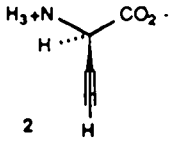
Abstract - The preparation of optically active, E-vinyl glycine derivatives is described. The bromoglycinate **4**, couples with trialkyltin acetylides in the presence of $ZnCl_2$ to furnish the *anti*-alkynes **5**. Dissolving metal reduction directly furnishes the N-t-BOC-protected E-vinyl glycine derivatives **6**.

The β,γ-unsaturated amino acids (**1**, Vinyl glycines) are an increasingly important class of α-amino acids. These interesting compounds from both natural and unnatural (ie., synthetic) sources have proven to possess antimicrobial[1] and enzyme inhibitory properties.[2] Specifically, several β,γ-unsaturated amino aicds have been shown to be suicide inactivators of several vitamin B_6-dependent enzymes such as alanine racemase, glutamate-aspartate transaminase, β-cystathionase, amongst others.[1,2] The β,γ-unsaturated amino acids have also proven useful as synthetic intermediates[3] and biochemcial probes.[4]



1



2

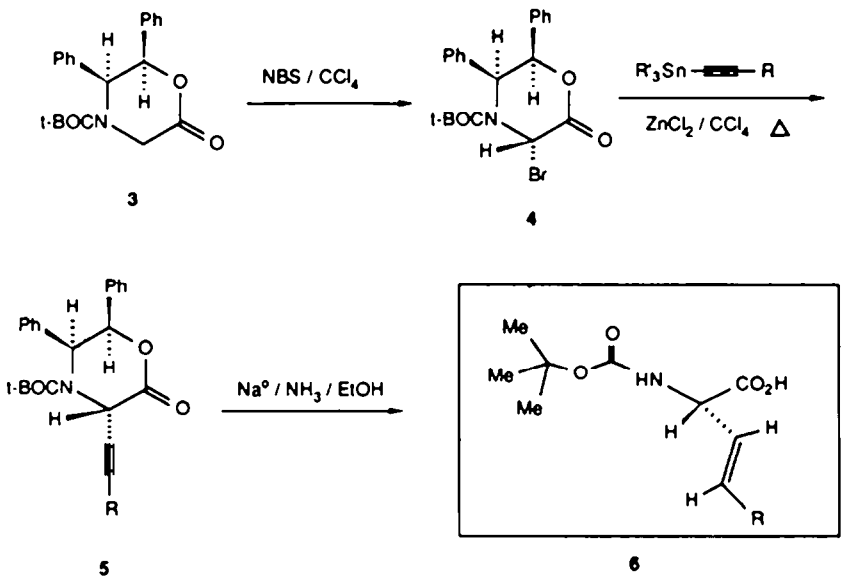
The closely related, unstable amino acid ethynyl glycine (**2**) has been isolated from a *Streptomyces sp.*[5] and has also been shown to possess antimicrobial activity as well as being a suicide inactivator of alanine racemase.[1a]

Syntheses of vinyl glycines has proven to be a challenging and difficult task, particularly in optically active form. This is primarily due to the lability of these substances toward racemization and, rearrangement of the unsaturated moiety into conjugation with the carboxyl group (ie., to α,β-dehydro amino acids). Numerous syntheses of *racemic* β,γ-unsaturated amino acids have been developed[6], but only a few successful methods for the preparation of optically active systems have appeared.[7] Enzymatic and other classical resolution procedures of the racemic substances are often attended by partial racemization and other side reactions. A noteworthy contribution has been developed by Schöllkopf and collaborators[8] who have found that aldol condensation of the optically active bis-lactim ethers of piperazinediones, followed by elimination and hydrolysis, furnishes a variety of substituted vinyl glycines with high enantiomeric excess. However, where double bond stereoisomerism is possible, this method[8] suffers from producing E/Z mixtures which must be subsequently separated.

As part of our continuing studies with the electrophilic glycine template (**4**)[9], we wish to record the first asymmetric, stereodefined and practical method to construct E-vinyl glycine derivatives. As shown in Scheme 1, bromoglycinate **4** couples[10] with trialkyl tin acetylides[11] under very mild conditions in good yield to furnish the crystalline, *anti*-adducts **5**. To the best of our ability, we have not been able to detect the corresponding

syn-diastereomers in any of these coupling reactions. Treatment of these alkynes with sodium metal in liquid ammonia/THF containing ethyl alcohol followed by a simple aqueous wash and filtration through a small plug of silica gel directly furnishes in good yield, the N-t-BOC-protected E-β,γ-unsaturated amino acids (**6**) in excellent chemical purity. The stereochemistry of the double bond was readily ascertained by examination of the vicinal olefinic coupling constants[12] which were typically J ~ 14.5-15 Hz. In no case, did we find evidence for the formation of any of the corresponding Z- isomers, nor was there evidence for formation of α,β-dehydro amino acids. The Table provides the data on yields for the coupling reactions (**3** → **5**), the dissolving metal reductions (**5** → **6**) and the % enantiomeric excess for each case thus far examined.

SCHEME 1



3 **4** **5** **6**

While the chemical yield in each case was quite good with Na° as the reductant, we found that partial racemization attended these reductions; the % ee was typically 55-67%. This was quite surprising since, the starting lactones **5** were single diastereomers of >98% ee and in no case did we observe α,β-dehydro amino acids or the fully saturated analogs. It would be expected that such by-products would result from the racemization of intermediates whether the process be base-catalyzed or free radical in nature.

When the reduction was performed with Li° in liquid ammonia/THF/EtOH, the derivatives **6** were produced in lower chemical yields, but higher optical purity (Table). The outstanding example being the E-dehydronorvaline (**6**, R=CH_3) which was obtained in >98% ee. The basis for the partial racemization of the other systems compared to dehydronorvaline is not at present, clearly understood. Efforts to elucidate the mechanism of the partial racemization with either Na° or Li°; and a means to attenuate this unwelcome phenomena are under intensive study.

TABLE 1

R	*% YIELD (5)* [a]	*% YIELD OF 6 via Na°*	*% ee via Na°*	*% YIELD OF 6 via Li°*	*% ee via Li°*	*J $H_{\alpha,\beta}$ of 6*
CH_3	61	70	64	18	>98	14.5
n-C_3H_7	65.5	80	61	20	72	15.0
n C_6H_{13}	61.2	74	56	16	65	14.9
$(CH_2)_2OSiMe_2$-t-Bu	71	71	68			14.9

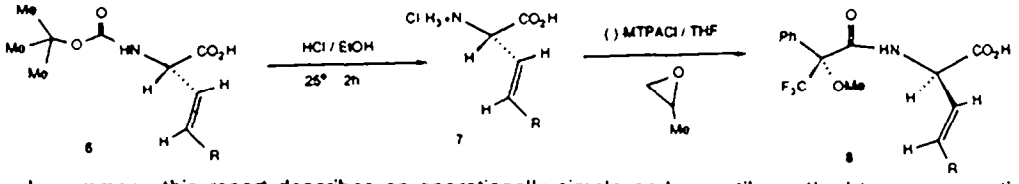
[a] Yields are for the two-step conversion of 3 → 4 → 5

In spite of the modest chemical yields employing lithium, the t-BOC amino acids **6** were operationally very simple to prepare and isolate. The reactions were typically quenched with NH_4Cl, the NH_3 was allowed to evaporate and the residue partitioned between water and ether. The aqueous layer was then acidified to

pH 3 and the t-BOC amino acids (6) were extracted and isolated by a simple silica gel filtration or PTLC separation.

The determination of the % ee proved to be somewhat difficult on the t-BOC derivatives (6) directly, and were therefore derivatized. Treatment of 6 with ethanolic HCl at room temperature for 2 h cleanly removed the t-BOC group resulting in the amino acid-hydrochloride salts 7. Acylation of 7 with (-)-MTPACl[14] furnished the amides 8 which were analyzed by ^1H and ^{19}F NMR to obtain the calculated % ee. Authentic samples of the racemic derivatives 7 and the corresponding diastereomers of 8 for comparison purposes were prepared from racemic 3. In these cases, the Na°/liquid ammonia protocol was utilized due to the higher chemical yields mentioned above.

SCHEME 2



In summary, this report describes an operationally simple and versatile method to prepare optically active E-vinyl amino acid derivatives in good chemical yield. The method can embrace a potentially large variety of γ-"R" groups that is dictated solely by the availability of the trialkyl tin acetylides. The availability[15] of both optical isomers of 3 provide the added flexibility of being able to prepare either the D- or L- configured vinyl glycine derivatives. Efforts to extend this chemistry to Z-vinyl glycines and higher substitution patterns around the double bond are in progress. It is expected that this method will find utility in numerous important applications in amino acid and peptide chemistry.

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EXPERIMENTAL

(3S,5S,6R)-4-tert-Butoxycarbonyl-5,6-diphenyl-3-(1'-propynyl)-2,3,5,6-tetrahydro-1,4-oxazin-2-one (5, R = -CH_3).

To a stirred refluxing solution of 3 (242 mg, 0.68 mmol, 1.0 eq) in CCl_4 (70 mL) was added N-bromosuccinimide (134 mg, 0.75 mmol, 1.1 eq). The mixture was allowed to reflux for 20 min, cooled to 0°C and filtered to remove succinimide. The filtrate was then brought to reflux temperature and tri-n-butyl propynyl stannane (293 mg, 0.89 mmol, 1.3 eq) and a solution of anhydrous $ZnCl_2$ (0.68 mL of a 1 M THF solution, 0.68 mmol, 1.0 eq) was added. The mixture was refluxed for 10 min, cooled to room temperature, diluted with H_2O (5 mL) and partitioned. The aqueous layer was further extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, concentrated and filtered through a short silica gel plug (CH_2Cl_2). The product was crystallized from the residue with hexane/CH_2Cl_2. 164 mg (61%). mp 221-223°C $[\alpha]_D^{25}$ = -37.9° (C, 0.78, $CHCl_3$). mp (racemic) 201-202°C.

^1H NMR (200 MHz, DMSO-d_6, 393°K) δ TMS: 1.2(9H,s); 1.9(3H,s); 5.13(1H,s); 5.6(1H,s); 6.4(1H,s); 6.6-7.3(10H,m). IR (NaCl, neat): 2295, 2220, 1780, 1715, 1610, 1500 cm^{-1}. mass spectrum (NH_3/Cl) m/z = 409($M^+ + NH_4^+$, 0.5); 392(M + 1, 0.3); 353(44); 292(12.9); 106(100). Anal. ($C_{24}H_{25}NO_4$) calcd. C, 73.64; H, 6.44; N, 3.58. found C, 73.37; H, 6.54; N, 3.52.

(3S,5S,6R)-4-tert-Butoxycarbonyl-5,6-diphenyl-3-(1'-octynyl)-2,3,5,6-tetrahydro-1,4-oxazin-2-one (5, R = n-C_6H_{13}).

To a stirred refluxing solution of 3 (286 mg, 0.81 mmol, 1.0 eq) in CCl_4 (70 ml) was added N-bromosuccinimide (159 mg, 0.89 mmol, 1.1 eq). The mixture was allowed to reflux for 20 min, cooled to 0°C and filtered to remove succinimide. The filtrate was then brought to reflux temperature and tri-n-butyl octynyl stannane (421 mg, 1.05 mmol, 1.3 eq) and a solution of anhydrous $ZnCl_2$ (0.81 ml of a 1 M THF solution, 0.81 m Mol, 1.0 eq) was added. The mixture was refluxed for 10 min, cooled to room temperature, diluted with water (5 ml) and partitioned. The aqueous layer was further extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, concentrated and filtered through a short silica gel plug

(CH_2Cl_2). The product was crystallized from the residue with hexane/CH_2Cl_2. 231 mg (61.8%), m.p. 145.5 ~ 146°C $[\alpha]_D^{25}$ = -23.8° (C, 0.16, CH_2Cl_2). m.p. (racemic) 120 ~ 122°C.

^{1}H NMR (200 MHz, DMSO-d^6), δ TMS: 0.82(3H, t, J=6.5Hz), 1.04 ~ 1.5(17 H, m), 2.33(2H, t, J=5.4 Hz), 5.25 ~ 5.30(1H, m), 5.67(1H, S), 6.42(1H, S), 6.54 ~ 7.33(10H, m). IR (NaCl, nujol) 2280, 2215, 1755, 1700 cm^{-1}. Mass spectrum (NH_3/Cl) m/z = 479(M^+ + NH_3, 0.7), 462(M^+, 0.4), 423(33.5), 362(100). Anal. ($C_{29}H_{35}NO_4$): calcd. C, 75.46; H, 7.46; N, 3.03. found C, 75.21; H, 7.42; N, 3.03.

(3S,5S,6R)-4-tert-Butoxycarbonyl-5,6-diphenyl-3-(1'-pentynyl)-2,3,5,6-tetrahydro-1,4-oxazin-2-one (5, R = n-C_3H_7).

To a stirred solution of **3** (270 mg, 0.76 m mol, 1.0 eq) in CCl_4 (70 ml) was added N-bromosuccinimide (150 mg, 0.84 mmol, 1.1 eq). The mixture was allowed to reflux for 20 min, cooled to 0°C and filtered to remove succinimide. The filtrate was then brought to reflux temperature and trimethyl pentynyl stannane (230 mg, 0.99 mmol, 1.3 eq) and a solution of anhydrous $ZnCl_2$ (0.77 ml of a 1 M THF solution, 0.77 mmol, 1.0 eq) was added. The mixture was refluxed for 10 min, cooled to room temperature, diluted with H_2O (5 ml) and partitioned. The aqueous layer was further extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, concentrated and filtered through a short silica gel plug (CH_2Cl_2). The product was crystallized from the residue with hexane. 210 mg (65.5%), m.p. 114 ~ 115°C, $[\alpha]_D^{25}$ = -26.8° (C, 0.22, CH_2Cl_2). m.p. (racemic), 131 ~ 131.5°C.

^{1}H NMR (200 MHz, DMSO-d^6), δ TMS: 0.91 ~ 1.09(9H, m), 1.42 ~ 1.57(5H, m), 2.28(2H, t, J=6.8 Hz), 5.26 ~ 5.33(1H, m), 5.68(1H, s), 6.41(1H, s), 6.54 ~ 7.26(10H, m). IR(NaCl, nujol): 2260, 2220, 1760, 1705 cm^{-1}. Mass spectrum (NH_3/Cl): m/z = 437(M^+ + NH^+_4, 0.5), 420(M^+ + 1, 0.4), 381(57.2), 364(18.5), 320(100). Anal. ($C_{26}H_{29}NO_4$) calcd. C, 74.44; H, 6.97; N, 3.34. found, C, 74.59; H, 6.82; N, 3.37.

(3S,5S,6R)-4-tert-Butoxycarbonyl-5,6-diphenyl-3-[((4'-tert-butyldimethylsilyl)oxy)but-1'-yne]-2,3,5,6-tetrahydro-1,4-oxazin-2-one (5, R = CH_2CH_2 OSi-Me$_2$-t-Bu).

To a stirred refluxing solution of **3** (200 mg, 0.57 mmol, 1.0 eq) in CCl_4 (70 ml) was added N-bromosuccinimide (111 mg, 0 62 mmol, 1.1 eq). The mixture was allowed to reflux for 20 min, cooled to 0°C and filtered to remove succinimide. The filtrate was then brought to reflux temperature and trimethyl (*tert*-butyl dimethylsilyl)oxy)butynyl stannane (256 mg, 0.74 mmol, 1.3 eq) and a solution of anhydrous $ZnCl_2$ (0.57 ml of a 1 M solution, 0.57 mmol, 1.0 eq) was added. The mixture was refluxed for 10 min, cooled to room temperature, diluted with H_2O (5 ml) and partitioned. The aqueous layer was further extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, concentrated and filtered through a short silica gel plug (CH_2Cl_2). The product was crystallized from the residue with hexane, 218 mg (71%), m.p. 128.5 ~ 129°C, $[\alpha]_D^{25}$ = -23.2° (C, 0.22, CH_2Cl_2). m.p. (racemic) 112.5 ~ 113°C.

^{1}H NMR (270 MHz, $CDCl_3$), δ TMS: 0.08(6H,S), 0.90(9H,S), 1.11(6H,S), 1.48(3H,S), 2.50(2H,t, J=6.8 Hz), 3.76(2H, t, J=6.9 Hz), 5.02 ~ 5.24(1H, m), 5.63 ~ 5.87(1H, m), 6.39 ~ 6.43(1H, m), 6.56 ~ 7.27 (10H, m). IR (NaCl, nujol): 2280, 2210, 1755, 1700 cm^{-1}. Mass spectrum (NH_3/Cl) m/z = 553(M^+ + NH_3, 1.1), 538(M^+ + 2, 0.4), 536(M^+, 0.2), 497(11.1), 480(17.8), 464(1.1), 436(24.6), 106(100). Anal. ($C_{31}H_{41}NO_5Si$): calcd. C, 69.95; H, 7.71; N, 2.61. found C, 69.72; H, 7.51; N, 2.66.

E-(2-tert-butoxycarbamoyl)pent-3-enoic acid (6, R = CH_3)

To a stirred solution of Na° (60 mg, 2.61 mmol, 17 eq) in NH_3 (2 ml, distilled from Na° at -33°C) was added a solution of **5** (R n=CH_3, 60 mg, 0.15 mmol, 1.0 eq.) and EtOH (200 µl) in dry THF (5 ml) via a syringe at -33°C. After 20 min the blue color disappeared, and the reaction was quenched with NH_4Cl. The mixture was allowed to warm. After the NH_3 was evaporated, the residue was diluted with water (10 ml) and extracted with Et_2O (2ml x 2). The aqueous layer was carefully acidified with 1N HCl to a pH of 3 while stirring with EtOAc. The layer was separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over anhydrous $MgSO_4$, filtered and evaporated to afford 26.1 mg (79%) of **6** as colorless oil.

$[\alpha]_D^{25}$ = + 52.2° (C, 0.68, CH_2Cl_2). % ee = 64%

^{1}H NMR (270 MHz, $CDCl_3$) δ TMS: 1 5(9H,S), 1.72(3H,d, J = 6.5 Hz), 4.8(0.5H, br.), 5.15(0.5 H, br.), 5.48 ~ 5.55(1H,m), 5.79 ~ 5.85(1H, m, $J_{Ha,b}$ = 14.5 Hz (decoupling)). IR (NaCl, neat). 3320, 2980, 2920, 1720, 1660, 1500, 1450 cm^{-1}. Mass spectrum (NH_3/Cl) m/z = 252(M^+ + 37, 0.2), 215(M^+, 1.4), 177(22.8), 159(29.3), 116(44.1), 70(100). Anal. ($C_{10}H_{17}O_4N$). calcd. C, 55.80; H, 7.96; N, 6.51. found C, 55.69; H, 8.00; N, 6.42.

To a stirred solution of Li° (6.9 mg, 0.997 mmol, 13 eq.) in NH_3 (20 ml, distilled from Na° at -33°C) was added a solution of **5** (R = CH_3, 30 mg, 0.077 mmol, 1.0 eq.) and isopropanol (150 µl) in THF (4 ml) via a

syringe at -33°C. The resulting mixture was stirred for 5 min., then quenched with NH_4Cl. The mixture was allowed to warm. After the NH_3 was evaporated, the residue was diluted with water (5 ml) and extracted with Et_2O (1.5 ml x 2). The aqueous layer was carefully acidified with 1N HCl to a pH of 3 while stirring with EtOAc. The layer was separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over anhydrous $MgSO_4$, filtered and evaporated to afford 3 mg (18%) of 6 as a colorless oil.

$[\alpha]_D^{25}$ = +61° (C, 0.23, CH_2Cl_2), %ee >98%.

E-(2-tert-butoxycarbamoyl)hept-3-enoic acid (6, R= η-C_3H_7).

To a stirred solution of Na° (30 mg, 1.29 mmol, 12 eq) in NH_3 (20 ml, distilled from Na° at -33°C) was added a solution of 5 (R = n-C_3H_7, 45 mg, 0.11 mmol, 1.0 eq) and EtOH (250 µl) in dry THF (5 ml) via a syringe at -33°C. After 20 min the blue color disappeared, and the reaction was quenched with NH_4Cl. The mixture was allowed to warm. After the NH_3 evaporated, the residue was diluted with water (8 ml) and extracted with Et_2O (2 ml x 2). The aqueous layer was carefully acidified with 1N HCl to a pH of 3 while stirring with EtOAc. The layer was separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and evaporated to afford 21 mg (80%) of 6 as a colorless oil.

$[\alpha]_D^{25}$ = +45.3° (C, 0.75, CH_2Cl_2). % ee = 61%.

^1H NMR (200 MHz, $CDCl_3$) δ TMS: 0.88(3H, t, J=7.3 Hz), 1.23 ~ 1.73(11H, m), 1.95 ~ 2.10(2H, m), 4.80(0.5H, br.), 5.14 ~ 5.16(0.5H, m), 5.44 ~ 5.53(1H, m), 5.77 ~ 5.85(1H, m, $J_{Ha,b}$ = 15.0 Hz (decoupling)), 10.2(1H, br.). IR (NaCl, neat): 3300(br.), 2960, 1715, 1650, 1500 cm^{-1}. Mass spectrum (NH_3/CI): m/z = 251(M^+ + NH^+_4, 0.2), 244(M^+ + 1, 0.3), 205(5.3), 187(9.4), 144(9.2), 126(22.3), 98(100). Anal. ($C_{12}H_{21}NO_4$). calcd. C, 59.24; H, 8.70; N, 5.76. found C, 59.02; H, 8.85; N, 5.57.

To a stirred solution of Li° (5.4 mg, 0.776 mmol, 13 eq.) in NH_3 (15 ml, distilled from Na° at -33°C) was added a solution of 5 (R = η-C_3H_7, 25 mg, 0.0597 mmol, 1.0 eq.) and isopropanol (150 µl) in THF (4 ml) via a syringe at -33°C. The resulting mixture was stirred at the same temperature for 5 min., then quenched with NH_4Cl. The mixture was allowed to warm. After the NH_3 was evaporated, the residue was diluted with water (5 ml) and extracted with Et_2O (1.5 ml x 2). The aqueous layer was carefully acidified with 1N HCl to a pH of 3 while stirring with EtOAc. The layer was separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, evaporated and separated on PTLC (silica gel, eluted with 7% MeOH/CH_2Cl_2) to afford 2.8 mg (19%) of 6 as a colorless oil. $[\alpha]_D^{25}$ = +31° (C, 0.28, $CDCl_3$), % ee = 72.2%.

E-(2 tert-butoxycarbamoyl)dec-3-enoic acid (6, R = n-C_6H_{13})

To a stirred solution of Na° (32 mg, 1.36 mmol, 12 eq) in NH_3 (20 ml, distilled from Na° at -33°C) was added a solution of 5 (R = η-C_6H_{13}, 52.4 mg, 0.1134 mmol, 1.0 eq) and EtOH (200 µl) in dry THF (5 ml) via a syringe at -33°C. The resulting mixture was stirred at the same temperature for 1 hr, then quenched with NH_4Cl. The mixture was allowed to warm. After the NH_3 was evaporated, the residue was diluted with H_2O (8 ml) and extracted with Et_2O (2 ml x 2). The aqueous layer was carefully acidified with 1NHCl to a pH of 3 while stirring with EtOAc. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, concentrated and separated on PTLC silica gel (eluted with 7% CH_3OH/CH_2Cl_2) to afford 23.9 mg (74%) of 6 as colorless oil.

$[\alpha]_D^{25}$ = + 7.5° (C, 0.32, CH_2Cl_2). % ee = 56%.

To a stirred solution of Li° (13.8 mg, 1.998 mmol, 13 eq.) in NH_3 (20 ml, distilled from Na° (at -33°C) was added a solution of 5 (R = η-C_6H_{13}, 71 mg, 0.154 mmol, 1.0 eq.) and isopropanol (200 µl) in THF (5 ml). The resulting mixture was stirred for 5 min. at the same temperature, then quenched with NH_4Cl. The mixture was allowed to warm. After the NH_3 was evaporated, the residue was diluted with H_2O (10 ml), extracted with Et_2O (2.5 ml x 2). The aqueous layer was carefully acidified with 1N HCl to a pH of 3 while stirring with EtOAc. The layer was separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, evaporated and separated on PTLC (silica gel, eluted with 7% MeOH/CH_3OH) to afford 7.1 mg of 6 as a colorless oil. $[\alpha]_D^{25}$ = +28.3° (C, 0.205, CH_2Cl_2), % ee = 65.4%.

^1H NMR (200 MHz, $CDCl_3$) δ TMS: 0.88(3H, t, J=6.4 Hz), 1.20 - 1.59(17H, m), 1.95 ~ 2.10(2H, m), 4.76 ~ 4.81(0.5H, m), 5.03 ~ 5.12(0.5H, m), 5.45 ~ 5.52(1H, m), 5.76 ~ 5.87(1H, m, $J_{Ha,b}$ = 14.9 Hz (decoupling). IR (NaCl, neat): 3300(br.), 2960, 1710, 1640, 1450, 1390, 1120 cm^{-1}. Mass spectrum (NH_3/CI): m/z = 303(M^+ + $Mt^+_4NH^+_4$, 0.3), 286(M^+ + 1, 0.4), 247(20.1), 229(71.1), 186(20.3), 140(100). Anal. ($C_{15}H_{27}NO_4$): C, H, N.

E-(2-tert-butoxycarbamoyl)-6-((tert-butyldimethylsilyl)oxy)-hex-3-enoic acid (6, R = $CH_2CH_2OSiMe_2t$-Bu).

To a stirred solution of Na° (50 mg, 2.14 mmol, 17 mmol) in NH_3 (20 ml, distilled from Na° at -33°C) was added a solution of **5** (R = -$CH_2CH_2OSiMe_2$t-Bu), 65 mg, 0.12 mmol, 1.0 eq) and EtOH(180 µl) in dry THF via a syringe at -33°C. After 20 min. the blue color disappeared, and the reaction was quenched with NH_4Cl. The mixture was allowed to warm. After the NH_3 was evaporated, the residue was diluted with water (10 ml) and extracted with Et_2O (2.5 ml x 2). The aqueous layer was carefully acidified with 1N HCl to a pH of 3 while stirring with EtOAc. The layer was separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over anhydrous $MgSO_4$, filtered and evaporated to afford 30.7 mg (71%) of **6** as colorless oil. $[\alpha]_D^{25}$ = + 11.2°(C, 0.5, CH_2Cl_2). % ee = 68%.

^{1}H NMR (200 MHz, $CDCl_3$) δ TMS: 0.018(6H, s), 0.85(9H, s), 1.42(9H, S), 2.21 ~ 2.31(2H, m), 3.62(2H, t, J=6.7 Hz), 4.79 ~ 4.81(0.5H, br.), 5.06 ~ 5.09(0.5H, br.), 5.58 ~ 5.61(1H, m, br.), 5.77 ~ 5.85(1H, m, $J_{Ha,b}$ = 14.9 Hz (decoupling)). IR (NaCl, neat): 3410, 3300, 2910, 2820, 1710, 1640, 1490, 1390, 1360 cm^{-1}. Mass spectrum (NH_3/Cl): m/z = 360(M^+ + 1, 0.9), 338(2.8), 321(4.9), 303(100), 286(25.8). Anal. ($C_{17}H_{33}NO_5Si$): calcd. C, 56.79; H, 9.25; N, 3.90. found C, 56.84; H, 9.30; N, 3.98.

General procedures for deprotection of the tert-butoxycarbamoyl groups and subsequent determination of % ee.

6 (0.01 ~ 0.06 mmol, 1.0 eq.) was treated with 1 ml of HCl/EtOH (1M solution), stirred at room temperature for 50 min., evaporated and dried in vacuo. to afford a residue. The residue was dissolved in dry THF, (-)MTPA-chloride (1.0 eq) and propylene oxide (4.0 eq.) were added. The resulting mxiture was warmed (40°C) for 20 min., evaporated and examination of the crude residue by ^{1}H NMR and ^{19}F NMR indicated the enantiomeric excess of **6**.

References and Footnotes

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11. WARNING: Extreme caution should be exercised when handling the highly toxic trimethyl tin compounds.
12. In each case, the olefinic coupling constant was determined by homonuclear decoupling.
13. Yields refer to purified, analytical samples.
14. MTPACl = α-Methoxy-α-(trifluoromethyl) phenylacetyl chloride.
15. Both optical isomers of **3** are commercially available from the Aldricih Chemical Co.